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THE USE OF ULTRAVIOLET RADIATION OF DIFFERENT SPECTRAL COMPOSITION FOR REDUCING THE SEQUELS OF RADIATION INJURY

/Following is a translation of an article written by Candidate of Medical Sciences T. A. Svid-erskaya, Scientific Associate Ye. C. Zhuk, and physician I. N. Filipson in Gigiyena i Sanitariya (Hygiene and Sanitation), Vol. 25, No. 2, Moscow, 1960, pages 27-33./

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The present study was undertaken to clarify the possibility of using ultraviolet radiation as a prophylactic measure in penetrating radiation injuries.

The work was carried out on 202 male guinea pigs, of 300 to 480 gm weight. Some of the animals were subjected to a single gamma-irradiation of 450r dose (control). Another group of animals had a course of prophylactic irradiation with ultraviolet (UV) rays in various doses nine to 14 days prior to gamma- ray irradiation (experiment). Radioactive cobalt (Co^{60}) served as a source of penetrating radiation. The force of radiation was 9.86 to 10.60 r per minute. To carry out prophylactic irradiations, we used sources of UV radiation of various spectral composition: luminescent erythema-lamps (EUV-15), of 280 to 380 micromicron radiation wave lengths, bactericidal lamps (BUV-15) of which the greater part of radiation has a 253 .7 micromicron wavelength, as well as the integral radiation stream of the usual mercury-quartz lamps of the PRK-2 type. The light emission intensity by the source of UV radiation was ascertained with an ultraviolet meter (UFM-5). The UV radiation was employed in total doses: 3.75, 7.5, and 15 biodoses (of a guinea pig) for a course of 10 daily treatments. Two variants of irradiation were carried out: the first -- by increasing the doses from 0.25 or 0.5 to 1.25 or 2.5 biodoses; the second -- with equal suberythemic doses (0.75 biodoses). Before the start of irradiation and after the fifth treatment, the fur on an area of 40 cm^2 of the animal's back was removed.

The blood of all animals selected for the experiment was examined three times, and subsequent blood examinations

were performed on the 2nd, 5th, 10th, 15th, 20th, 25th, 30th day, etc., following irradiation. The cholinesterase activity of the blood was determined by the method of S. R. Zubkova and T. V. Pravdich-Neminskaya in the M. Ya. Mikhel'son modification. The work capacity of the animals was studied on "tretban" [a treadmill?] of special construction. As the basis of the method of work capacity determination, a conditioned motor-defense situation reflex was used. As unconditioned reinforcement, thermal skin stimulation was used. The work effected by the animal was represented by running on a horizontal conveyer strip of a transporter. During the entire experiment continuous observations were also conducted on the changes of the morphological composition of the blood, cholinesterase activity, and the dynamics of weight in a group of healthy animals (biological control) which had been kept under similar conditions of maintenance and food regimen as these of the experimental animals.

A total of four series of experiments were carried out (Table 1).

Table 1

Characteristics of the experimental series

Series	Source of UV irradiation	Number of animals	Total dose of UV radiation (biodose)	Dose of gamma irradiation (r)
I	EUV-15	50	7.5 and 15	400
II	EUV-15	20	7.5 and 15	450
III	BUV-15	50	7.5 and 15	450
IV	PRK-2	82	3.75; 7.5 and 15	450

A single total gamma-irradiation with a 450 r dose induced in guinea pigs of an average weight of 430 gm an acute radiation sickness of III and II degree of gravity. Starting on the third or fourth day, following gamma-irradiation, the motor activity and the food excitability of the animals became lower. During the height of the disease a pronounced adynamia, refusal of food, hemorrhages in the oral mucose membrane, and feces mixed with blood were observed. Toward the eighth to 12th day following gamma-irradiation, the majority of the animals perished with phenomena of marked emaciation. The acute radiation sickness was accompanied by a profound impairment of the normal hemopoie-

sis. Toward the second day, following gamma-irradiation, the number of leucocytes decreased by 50 percent, and toward the fifth day it was 90 percent lower than the initial level. The absolute number of leucocytes fell to 500 to 750 in one mm^3 of blood. The reduction in the number of erythrocytes began on the second or third day. Toward the 15th day of the disease the number of erythrocytes fell, on the average, to 35 percent (1,155,000 cells in one mm^3) and the hemoglobin content to 36 percent of the initial level. The number of reticulocytes showed a marked decrease within the first few days following the effect of penetrating radiation, and toward the fifth day constituted one percent of the initial figure. The reticulocytes disappeared completely in the peripheral blood on the 10th day. Also under gamma-irradiation the activity of blood cholinesterase was considerably inhibited: it constituted, on the average, 34 percent of the initial level (in some animals -- up to 22 percent). A gradual restoration of cholinesterase activity took place in the surviving animals starting on the 10 - 15th day of the disease.

A preliminary irradiation of guinea pigs with UV rays in our experiments increased the resistance of their organism to the subsequent effect of penetrating radiation. Prophylactic irradiation attenuated the course of the acute radiation sickness; the number of instances of III degree gravity was reduced, the height of the disease commenced four to five days later; there was a marked increase of the survival capacity of the animals and of the average life span, and a smaller loss of weight; and the tolerance of higher physical loads by the animals was higher. The indices of the morphological composition of the white and red blood, as well as the cholinesterase activity, did not reach such a low level in these instances.

In the mobilization of protective mechanisms which lay at the base of the prophylactic effect of UV rays, of substantial importance were the spectral composition and the size of the total dose of UV radiation, the length of time interval between the effect on the organism of both agents, as well as the methods of UV irradiation.

In Figure 1 are shown the survival data. Of 43 guinea pigs of the control group (gamma-irradiation) only three survived (6.7 percent), whereas in the group, which had received UV rays plus gamma-irradiation, of 89 animals 20 survived (22.5 percent).

The data on the effectiveness of the use of UV rays of various spectral composition, according to the survival data, are cited in Table 2.

Table 2

Survival rate of the control and experimental animals

Series	Character of irradiation	Source of UV irradiation	Number of animals		
			Total	Survived	
				Number	Percentage
II	gamma-irradiation	--	10	1	10
	UV rays + gamma-irradiation	EUV-15	10	3	30
III	gamma-irradiation	--	10	0	0
	UV rays + gamma-irradiation	BUV-15	30	3	10
IV	gamma-irradiation	--	25	2	8
	UV rays + gamma-irradiation	PRK-2	49	14	28.6
	Total gamma-irradiation	EUV-15	45	3	6.7
	UV rays + gamma-irradiation	BUV-15 PRK-2	89	20	22.5

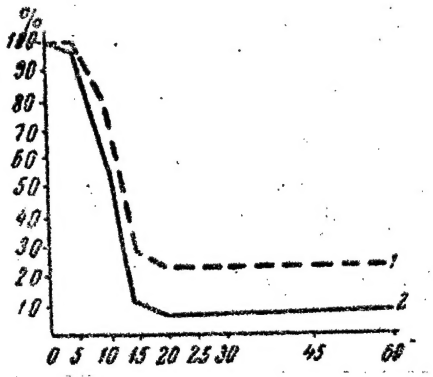
The highest survival rate was noted in animals which had been exposed to prophylactic irradiation with long-wave UV rays and integral radiation of the PRK-2 burner (30 percent and 28.6 percent, respectively). During the two-month period of observation the average life span of a control animal was 13.9, and in the experiment -- 25.2 days.

The character of changes and their direction, established in the analysis of survival and life span of experimental animals coincide with the data of study of the morphological composition of the peripheral blood and the cholesterinase activity. The most marked leukopenia was noted on the fifth to tenth day of the disease, when the number of leucocytes in the animals of the control group

fell to 13-11 percent, and in the group of animals who had received UV + plus gamma-irradiation -- to 16-14 percent. The restoration of the number of leucocytes commenced (the data relate to animals who had survived) on the tenth day following gamma-irradiation. In the animals of the control group, the restoration process reached the 59-65 percent level, but did not revert to the initial figure for two months. In the group of animals who had received UV + gamma-ray irradiation the restoration of the number of leucocytes proceeded continuously and on the 45th day their number constituted 95 percent, and on the 60th day -- 110 percent of the initial figure.

The dependence of the leucocytic reaction on the spectral composition of the UV radiation used for prophylactic irradiation is shown in Figure 2. As seen from it, the distinct differences, according to this indicator, are manifested during the recovery period only. The restoration process of the leucocyte count proceeded most rapidly in the group of animals subjected to long-wave UV ray irradiation, and was completed toward the end of the first month, following gamma-irradiation. In animals irradiated with bactericidal lamps the number of leucocytes, having reached the 82 percent level of the initial figure toward the 25th day, commenced to fall, and fluctuated, during the subsequent period, within 26-46 percent limits. The restoration curve of leucocytes in animals irradiated with the integral source of PRK-2 radiation lamp occupies a medium position on the diagram. Thus, the most favorable effect on the course of restoration of the leukopoietic function is exerted by radiation of the EUV-15 lamp. Prophylactic irradiation with shortwave rays showed no positive effect on the course of these reparation processes.

The most pronounced protective effect of UV rays was manifested in the red blood system. Here, the differences manifested themselves not only during the restoration period, but also in the course of radiation sickness. The reduction in the number of erythrocytes and hemoglobin content in the experimental animal groups occurred later and was less pronounced (Fig. 3). The erythema lamps and the PRK-2 burners possessed a distinctly positive radiation effect. In animals irradiated with long-wave UV rays (EUV lamp), during the first two to five days following gamma-irradiation there was not only an absence of reduction of the number of erythrocytes observed, but even a certain increase. In animals subjected to the effect of bactericidal radiation, the maximum level of erythrocyte reduction was 44 percent, and in animals subjected to the effect of PRK-2 burner radiation it reached 47 percent of



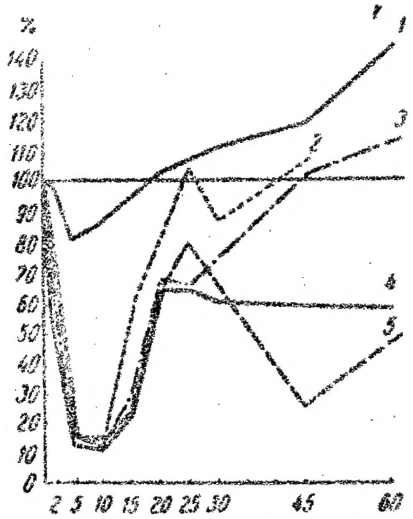
Days following gamma-irradiation

Fig. 1. Survival of guinea pigs subjected to the effect of penetrating radiation after preliminary irradiation with UV rays.

1 -- irradiation with UV rays and gamma-irradiation;
2 -- irradiation with UV rays (control).

the initial figure. The restoration process in animals subjected to the EUV and PRK lamp radiation also proceeded in a shorter period of time. Analogous results were obtained in the analysis of data on the changes in hemoglobin content. Thus, the most favorable effect on the state of hemopoiesis was achieved by irradiation with the long-wave stream of UV rays. In animals subjected to the effect of short-wave UV radiation, the number of erythrocytes during the recovery period was even lower than in the control group.

The preliminary UV irradiation of animals also altered the reaction on the part of the cholinergic systems of the organism to subsequent gamma-irradiation. The restoration of the activity of the enzyme

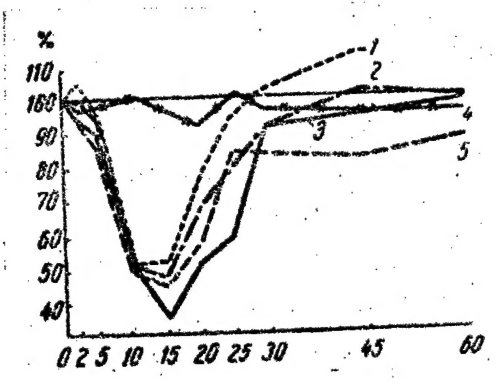


Days following gamma-irradiation

Fig. 2. Change in the number of leucocytes in the blood of guinea pigs under the effect of penetrating radiation, depending on the character of preliminary irradiation with UV rays (in percentages of the initial figure).

1 -- biological control;
2 -- irradiation with UV rays (EUV lamp) and gamma-irradiation;
3 -- irradiation with UV rays (PRK lamp) and gamma-irradiation;
4 -- gamma-irradiation (control);
5 -- irradiation with UV rays (BUV lamp) and gamma-irradiation.

in animals, subjected to the effect of the bactericidal and integral stream of radiation, proceeded much more rapidly than in animals of the control group, but at later periods than in animals subjected to the effect of long-wave UV radiation.



Days following gamma-irradiation

Fig. 3. Change in the number of erythrocytes in the blood of guinea pigs under the effect of penetrating radiation depending on the character of preliminary irradiation with UV rays (in percentages of the initial figure)

1 -- irradiation with UV rays (EUV lamp); 2 -- irradiation with UV rays (PRK lamp); 3 -- gamma irradiation (control); 4 -- biological control; 5 -- irradiation with UV rays (BUV lamp).

The cited data attest to the fact that the effectiveness of the use of UV rays is most closely connected with the spectral composition of the acting source. Analysis of the obtained data also shows that in the prophylactic effect of UV rays a substantial role is played by the size of total dose, and that the quantity of the optimum prophylactic dose of UV radiation depends on its spectral composition. In our experiments with the employment of long-wave UV radiation the increase of the total UV radiation dose from 7.5 to 15 biodoses led to the enhancement of the prophylactic effect. In contrast, in the employment of the integral radiation stream of the PRK-2 burner and bactericidal rays of the BUV lamp, an increase of the

total dose from 3.75 to 15 biodoses was accompanied by a reduction of the prophylactic effect. This is confirmed by the data on the survival of animals and the data of changes which occur in all investigated functional systems.

Upon the employment of PRK-2 lamp, in nine out of 14 survivor-animals the total dose of UV rays constituted 3.75 biodoses, and in five -- 7.5 biodoses. An increase of the total dose of UV radiation to 15 biodoses, with the use of PRK-2 and PUV lamps, reduced the survival capacity of the animals.

As is known, in the consecutive action of several physical factors on the organism, particularly when higher doses are employed, definite time intervals between such actions should be observed. In order to ascertain the role of time intervals between the action of UV rays and penetrating radiation, the gamma-irradiation in our experiments was conducted within nine to 14 days after the termination of prophylactic irradiation. The result was that, at an equal UV rays dose, the increase of this interval enhances the survival capacity of the animals and improves the clinical course of the disease; these effects are reflected in lesser reduction of the number of erythrocytes, the quantity of hemoglobin, and other indices (Table 3).

As seen from Table 3, during the sixth to tenth day of the disease of animals irradiated with the integral stream of UV rays (PRK-2), at an interval of nine days, of 14 guinea pigs survived only seven, and, at an interval of 14 days, of 35 survived 28 animals (80 percent). There was also an increase in the survival capacity of the group of guinea pigs irradiated with UV bactericidal rays. It is necessary to underline that survival in this group, especially with the interval of nine days, was the lowest.

The dependence on the time interval is also seen from the analysis of the number of erythrocytes and cholinesterase activity (Figs. 4 and 5).

The results of the experiments of the IV series (the most numerous) showed that, in the mobilization of the protective mechanisms which constitute the basis of the UV rays effect, of definite importance is also the method of employing UV radiation on the organism.

To obtain a biological effect, it is quite a different matter whether the total UV dose is administered in small portions or is being increased with each successive treatment. It was found that the death rate of guinea pigs was lower, when the UV irradiation was carried out with equal non-erythemic doses, than in irradiation with progressively higher doses. In irradiation with equal doses, 10 animals out of 17 survived; in irradiation with progress-

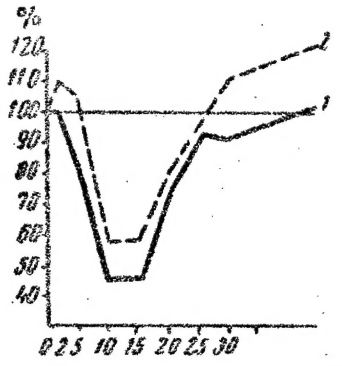
Table 3

Survival rate of the animals and the time interval between irradiation with UV rays and gamma-rays

Interval (in days)	Source of UV radiation	Number of Animals	Survival rate (in days of the disease			
			6 -- 10th		11 -- 30th	
			number	%	number	%
9	BUV-15	15	14	92.4	1	6.6
	PRK-2	14	7	50	5	21.5
	Total	29	21	72.4	6	20.7
14	BUV-15	15	13	86.7	4	26.7
	PRK-2	35	28	80	16	45.7
	Total	50	41	82	20	40

ly higher doses four out of 28 animals survived. This phenomenon could be traced in the study of other biological indices. Thus, when a permanent dosage was used at a total UV dose of 7.5 biodoses, the cholinesterase activity rose to 114 percent of the initial figure on the second day following irradiation. Subsequently, activity was reduced, reaching its maximum level of 67 percent on the 10th day. In animals which had received the same total dose but had been irradiated with progressively increasing doses, the cholinesterase activity fell immediately following irradiation, and on the 10th day constituted 49 percent of the initial figure.

The study of tolerance to physical loads was carried out in only the first series of experiments on animals irradiated with long-wave UV rays, within two months following their gamma-irradiation. As shown by observations, healthy guinea pigs (biological control) were able, on the average, to carry out work of 0.83 kg per second (100 percent), whereas the tolerance to a physical load in animals which had been irradiated with radioactive cobalt and suffered radiation sickness was equal to 0.65 kg/sec (78.3 percent) only. Thus, their work capacity fell 21.7 percent. Guinea pigs, subjected to a preliminary UV-ray irradiation (total dose 7.5 biodoses), could carry out, on the average, 0.756



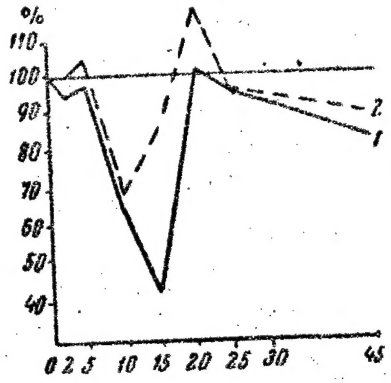
Days following gamma-irradiation

Fig. 4. Change in the number of erythrocytes in the blood of guinea pigs under the effect of penetrating radiation after preliminary irradiation with UV rays (EUV-15 lamp)

1 -- irradiation with 7½ biodoses and gamma-irradiation (on the 14th day); 2 -- irradiation with 15 biodoses and gamma-irradiation (on the 14th day).

kg work per second (91.1 percent), i. e., the reduction of work capacity of these animals within two months following gamma-irradiation constituted only 8.9 percent.

It is important to underline the fact that a definite correlation exists between all indices investigated above. In animals, who, after a preliminary UV irradiation, showed a smaller reduction of work capacity, similar changes were observed in a number of other indices: the reduction in the number of erythrocytes and hemoglobin was less pronounced, and the cholinesterase activity did not go below 40 percent, as compared to initial figures. In contrast, animals with lower work capacity also showed more pronounced changes in the morphological composition of the blood



Days following gamma-irradiation

Fig. 5. Change in the cholinesterase activity in the blood of guinea pigs under the effect of penetrating radiation after preliminary irradiation with UV rays (EUV-15 lamp).

1 -- irradiation with $7\frac{1}{2}$ biodoses and gamma-irradiation (on the 14th day). 2 -- irradiation with 15 biodoses and gamma-irradiation (on the 14th day).

and the cholinesterase activity.

Conclusions

1. Experiments on guinea pigs demonstrated that prophylactic use of UV rays increases the resistance of the organism to the effect of lethal doses (450 r) of gamma-radiation.

2. In animals subjected to prophylactic irradiation with UVR there is an increase in the survival rate, a considerably lesser reduction in the number of leucocytes, hemoglobin content, and cholinesterase activity, a lesser reduction of work capacity, and accelerated and more complete reparation processes.

3. In the mobilization of the defense mechanisms which are at the base of the prophylactic action of UVR, of substantial importance is the spectral

composition and size of the total dose of UV radiation, the length of time interval between the actions of both agents on the organism, as well as the method of UV irradiation.

4. The size of the optimum prophylactic dose of UV radiation depends on its spectral composition. Upon the increase of the total dose of erythemic radiation from 7.5 to 15 biodoses, the prophylactic effect of UV rays increases, while the increase of the total radiation dose of PRK-2 lamp (from 3.75 to 15 biodoses) and bactericidal lamps from 7.5 to 15 biodoses leads to the reduction of the prophylactic effect.

5. In the comparative evaluation of the prophylactic effect of UVR of various spectral composition used in equal biological doses, the long-wave radiation of EUV lamp and the integral stream of PRK-2 burner possess a greater protective effect as compared to the short-wave rays of BUV lamp.

6. Equal total doses of UV radiation exert a different protective effect, depending on the size of the time interval between the end of UV irradiation and the subsequent action of gamma-rays. The results of prophylactic irradiation were better at a 14-day interval, than at an interval of nine days.

7. The methods of carrying out the prophylactic irradiation has a definite effect on the final result. The PRK lamp radiation exerts a greater protective effect when the animals are irradiated with equal non-erythemic doses, and not with progressively higher doses.

8. The data cited in this work attest to the fact that, under definite conditions, UV rays may be used for the purpose of increasing the resistance of the organism to penetrating radiation.

Submitted 27 April 1959

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